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Data on adults included 644 (598 allo + 46 auto) evaluable patients out of total 835 patients reported. In pediatric cohort 165 patients suffered from malignancies, 356 patients were transplanted for non-malignant diseases; 437 underwent a first SCT, 87 had a subsequent transplant. In adult group 626 were treated for hematological malignancies and 18 for non-malignant diseases (SAA or thalassemia). No data on auto-SCT in adults were published after 2004. The majority of pediatric patients received treosulfan in dose 39-45 mg/m2 (332 patients, 62%). Most of adult patients treated after 2007 received dose of 42 mg/m2.

Results: The main indications for treosulfan use in pediatric population were non-malignant diseases (68%) or second SCT, while among adults older age (>50 years) and/or comorbidities disqualifying from myeloablative conditioning. No correlation between the given treosulfan dose and the grade III/IV toxicity was observed both in children and in adults. No association between dose and GVHD, OS, DFS, relapse incidence and TRM was found both in children and in adults.

Conclusions: Treosulfan-based conditioning with its low toxicity profile and dose-dependent myelotoxicity is a good option in children treated with non-malignant diseases. Additionally, both children and adults not eligible for conventional transplant regimen can be offered this treatment with acceptable results. Toxicity and survival were similar in children and adults, while acute and chronic GVHD incidence were higher in adult population.

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Rarity of Donor-Derived Malignancy after Allogeneic BMT with High-Dose Post-Transplantation Cyclophosphamide

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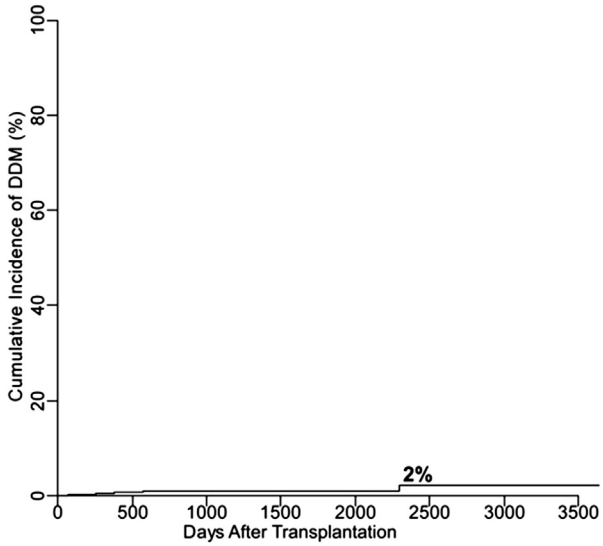
Donor-derived malignancy (DDM) is a rare but often fatal complication of alloBMT, with a reported incidence of 0.1-5%. AlloBMT utilizing high-dose post-transplantation cyclophosphamide (PT/Cy) as GVHD prophylaxis produces excellent rates of engraftment and low rates of acute and chronic GVHD. Because exposing the allograft to cytotoxic chemotherapy may theoretically increase the risk of DDM, we evaluated the incidence of DDM after alloBMT with PT/Cy. From 2000-2012, 790 patients (median age 51y, range 1-74y) received T-cell replete alloBMT with high-dose PT/Cy at Johns Hopkins, including 313 (40%) who received PT/Cy as sole GVHD prophylaxis. Of these transplants, 349 (44%) were HLA-haploidentical and 346 (44%) were myeloablative. Median donor age was 41y (range 13-79y). With a median follow-up of 3y (range, 0.8-9.4y) in patients without events, the 3 year PFS and OS probabilities were 42% and 56% respectively. Five cases (5/790=0.6%) of DDM were identified



as well as one case of clonal, donor-derived LGL leukemia that resolved without any therapy. By competing-risk analysis, the probability of DDM was 0.6% at 1 y, 0.8% at 5 y, and 2% overall (Figure). In the 5 identified cases of DDM, the median patient age was 41y (range 18-65 y) at BMT and median donor age was 41y (31-67y). These patients were initially transplanted for ALL (1), NHL (3), or Hodgkin lymphoma (1). Two patients received myeloablative conditioning and 3 received additional GVHD prophylaxis with mycophenolate mofetil and tacrolimus. The median time from BMT to the diagnosis of DDM was 1.3y (range 0.5-6.3y). DDMs consisted of MDS (1), AML (3), and CMML (1). All of the patients received treatment for their DDM; 2 are long term survivors and 3 died of their DDM. The incidence of developing a DDM after high-dose PT/Cy is rare, and is within the range reported for other transplant platforms.

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Ex −Vivo T Cell Depleted Allogeneic (TCD) Hematopoietic Stem Cell Transplantation for Advanced Chronic Myelofibrosis: MSKCC Experience

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Introduction: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only potentially curative treatment option for MF. The role of ex −vivo TCD allo-HSCT hasn't been reported in patients with advanced MF.

Patients: Between 5/1990-4/2013, 12 pts underwent TCD transplant at MSKCC for MF; 9 had primary MF, 2 post ET and 1 post MDS. Median age was 56 (42.7-65.5). Disease status prior to transplant per DIPSS was: intermediate-1 (4), intermediate-2 (6), and high-risk (2). Splenectomy prior to transplant was performed in 8 patients. JAK2 V617F mutation status was known on five patients and was detected on 3. Five pts received a TCD marrow graft and were conditioned with a TBI-based regimen and 7 pts received TCD peripheral blood graft and were conditioned with a chemotherapy

regimen consisting of busulphan, melphalan and fludarabine. All patients received ATG to prevent graft rejection. Donors were matched related (8) and matched unrelated (4). BM grafts were depleted of T-cells using the soybean agglutinin method followed by sheep RBC rosetting, and PB grafts by immunomagnetic CD34+ selection (Isolex initially and CliniMACS after 09/2011).

Results: Three pts died early and were not evaluable for engraftment, the remaining 9 pts engrafted. None of these pts developed acute or chronic GvHD after the primary graft. Of the 9 pts evaluable for long term follow up, 8 are alive with a median follow up time of 12.1 months (3.3-196 months). One pt relapsed 15 months post initial transplant and achieved remission after DLI. This patient developed acute gut GVHD that responded to steroids. Two additional pts received low dose DLI ($0.5x10^6$CD3 cells/kg), one for recurrent viral infections and the other as prophylaxis for relapse. These 2 pts had no GvHD post-DLI. Out of the 4 pts who did not undergo pre-transplant splenectomy, one required post transplant splenectomy for severe persistent thrombocytopenia which resolved post splenectomy. JAK2 mutation was not detected post transplant in any of the 3 pts.

In this small series of pts, eight out of twelve, 66%, are alive; two of the five pts in the subgroup cyto-reduced with TBI based regimen and six of the seven patients in the subgroup cyto-reduced with chemotherapy only regimen. The causes of death were: toxicity of the preparative regimen (TBI) in 2, intra-cranial hemorrhage in 1 and unknown in the 4 thpatient who died more than 2 years post transplant with no evidence of disease.

Conclusions: TCD transplantation can offer long term cure for patients with advanced chronic MF and with no evidence of GvHD in this small cohort of patients. The early experience at MSKCC with TCD transplant was associated with high rates of early mortality likely related to the high intensity conditioning regimen containing TBI. The current regimen of busulphan, melphalan, fludarabine and ATG has been well tolerated and the majority of pts are alive and disease free.

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Prospective Multicenter Phase II Study of Myeloablative Conditioning Consisted of Intravenous Busulfan and Fludarabine +/- Total Body Irradiation for Older Patients (55 years and older): Final Analysis of the JSCT FB09 Study

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Aim: Multicenter phase II study has been conducted to investigate whether myeloablative dose of intravenous busulfan (ivBu) can be used for elderly recipients.

Method: This study started in September 2009, and 32 centers participated (Trial identifier: UMIN000002426). Patients aged from 55 to 70 with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) who were planned for allo-SCT (bone marrow (BM), peripheral blood (PB), and cord blood (CB)) were enrolled. Pretransplant conditioining consisted of 30 mg/m2 of fludarabine (Flu) for 6 days (total 180 mg/m2) and 3.2 mg/kg of ivBu for 4 days (divided by 4 daily, total 12.8 mg/kg) with or without total body irradiation depending on type of donor cells. Calcineurine inhibitors + methotrexate for BM or PB recipients, and tacrolimus + mycophenolate mofetil were used for CB recipients.

Result: Thirty-eight patients were enrolled. Median age was 60 (55-68), 22 male and 16 female, 31 AML and 7 MDS were included. Donors were 8 matched and 2 1-Ag/allele-mismatched related BM/PB, 8 matched and 4 1-Ag/allele-mismatched unrelated BM, and 16 CB ($\leq$2-Ag-mismatched). There was 1 whose total dose of ivBu was reduced (11.2 mg/kg) due to neurotoxicity (grade III). Thirty-five achieved neutrophil recovery (median day 17 (range, 11-45)). There was 1 who died from NRM early before engraftment (CB recipient, day 27) due to cerebral hemorrhage, and were 2 who failed to engraft (both CB recipients, one due to early relapse, and the other due to rejection). There were 2 VOD/SOS observed. Cumulative incidences of grade II-IV and III-IV acute GVHD were 37% and 16%, respectively. With respect to donor type, no grade III-IV acute GVHD was observed in transplants from matched related donors. Cumulative incidence of total chronic GVHD was 38%. Up to 24 months post-transplant, there were 11 relapse, and 7 non-relapse mortality. Cumulative incidences of non-relapse mortality and relapse at 2-year post-transplant were 21% and 31%, respectively. Overall and event-free survivals were estimated to be 58 % and 53 % at 2 year post-transplant.

Conclusions: Myeloablative conditioning using Flu/ivBu12.8 mg/kg +/- TBI was well tolerated with acceptable low toxicities and was sufficient to allow donor cell-engraftment post allo-SCT for elderly patients with AML or MDS. Given the promising results of OS and PFS, phase II studies in much larger scale are now under investigation.

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Characteristics and Outcomes of Influenza a Infection in Hematologic Malignancy (HM) Patients and Hematopoietic Stem Cell Transplant

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Background: Influenza is one of the most common virus causing respiratory tract infection in HM patients and HSCT recipients. Severely immunocompromised pts suffer more severe disease, prolonged viral shedding, emergence of resistance as well as higher mortality rate. Studies comparing characteristics and outcomes of pandemic H1N1 and